Scientific Abstract

A PHASE I TRIAL OF A CEA-TRICOM BASED VACCINE AND RADIATION TO LIVER METASTASIS WITH OR WITHOUT CELECOXIB IN PATIENTS WITH CEA POSITIVE SOLID TUMORS

Background

Metastasis from a solid tumor to the liver usually portends a poor prognosis. Carcinoembryonic antigen (CEA) is overexpressed in virtually all adenocarcinomas of the colon and rectum and is used as a serologic marker of disease progression. It is also present on most adenocarcinomas of the breast, lung, pancreas, and other carcinomas. In light of the fact that current therapeutic strategies have had limited success in the metastatic disease setting, vaccine strategies represent an alternative approach to therapeutic intervention. Our current generation of vaccine, designated CEA-TRICOM, contains the transgenes for CEA as well as three costimulatory molecules. Clinical experience with CEA vaccines have demonstrated safety, superiority of a prime and boost schedule and clinical activity with significant correlation between CEA-specific T-cell responses and apparent clinical benefit. In addition, it has been shown that radiation can upregulate Fas expression on tumor cells and potentiate T-cell mediated killing of tumor. COX-2 inhibitors such as celecoxib not only have been shown to potentiate the anti-tumor response to our vaccine in preclinical models, but are radiosensitizers and can have synergistic anti-tumor responses when combined with radiation.

Objective/hypothesis

The overall objective of this study is to evaluate the safety and toxicity profile of the combination of a CEA-based vaccine and radiation with or without celecoxib in patients with CEA-positive solid tumors metastatic to the liver.

Study Design

Twelve patients will be enrolled in two sequential cohorts. The first cohort (n = 6) will receive a priming vaccination with rV-CEA-TRICOM vaccine followed with 4 sequential bi-monthly booster vaccinations of rF-CEA-TRICOM along with external-beam radiation therapy to the liver lesion(s). The radiation dose and schedule is designed to induce immunomodulatory effects (such as upregulation of Fas) and thus augment the T-cell mediated tumoricidal activity induced by the vaccine. The second cohort (n = 6) will receive celecoxib in addition to the same vaccine and radiation regimen as in the first cohort. All patients who remain on study will receive monthly booster vaccinations after completion of radiation therapy.

Relevance

This trial aims to obtain safety data on the use of a CEA-based vaccine and radiation to liver metastasis with or without celecoxib in patients with metastatic CEA-bearing solid tumors. If this trial is successful, future trials can be designed to evaluate clinical efficacy of this regimen in patients with advanced CEA-positive malignancy.